APh161: Physical Biology of the Cell
Homework 2
Due Date: Tuesday, January 23, 2007

"To arrive at the truth it is necessary, at least once in life, to rid oneself of all the opinions one has received, and to construct anew, and from the fundamentals, all the system's of one's knowledge." – R. Descartes

A. Reading and Refereeing

This week you will be asked to do quite a bit of reading and to write referee reports. Please take this seriously.

(a) Read the article on the website that we are planning on submitting to the *American Journal Physics* entitled "A First Exposure to Statistical Mechanics for Life Scientists". Write a referee report in which you give general comments on how this article might be improved. In addition, make a list of specific comments. Make sure to comment on your views of the extent to which this article would serve as an introduction to statistical mechanics for first-time statistical mechanicians. Also, comment on how well the article motivates the need for statistical mechanics in biology.

(b) To develop your skills in using the two-state formalism introduced in the paper, consider a protein that can exist in two states (active and inactive) and also, can exist in a phosphorylated or unphosphorylated state. The act of phosphorylation tunes the relative probability of active and inactive states. Make a states and weights diagram for the four possible states of the protein molecule and use *two* different two-state variables to characterize each of the states.

(c) Read chap. 2 of "Physical Biology of the Cell" and write a referee report in the spirit of the referee report that we have posted on the website.

1. Viruses and the Size of Things

(a) Estimate the number of protein units that make up a viral capsid for influenza virus. In addition, estimate the number of lipid molecules associated with one of these viruses. The lipid molecules surround the protein coat in lipid bilayer form. Make sure you show a picture of the virus and give a rough description of what the structure is like - where is the nucleic acid, what is the shape, etc.. Also, describe the genome of this virus and compute the total length of the nucleic acid molecules if they were strung together one after the other.

(b) Use fig. 1 of the paper by Briggs *et al.* on HIV that is posted on the course website to measure the dimensions of the immature HIV virion. Based on what you know about the makeup of the virion, estimate the number of lipids and the number of Gag proteins in the immature virion. Then, consider the mature virion and using fig. 2 of the second paper by Briggs *et al.* estimate the number of proteins in the ice-cream-cone-shaped capsid. How does your estimate for the number of proteins in the capsid compare to your estimate for the number of Gag proteins?

2. A Feeling for the Numbers: The Rates of Things

In the previous homework, we worked hard to get a sense for the physical sizes of various biological entities. Another interesting angle on all of this is to try and get a feel for the *rates* at which things happen. Following in the tradition of the previous problems, here you will try to make some estimates of the rates of some processes. Much of what you will do in this problem I have already done partially in class - your job is to make it your own now.

(a) Consider the division of an *E. coli* cell. Think of such a cell during rapid growth phase where the cell is dividing roughly once every 20 minutes. Make estimates of the number of water molecules being taken on board per second during this phase, the number of lipid molecules that are being added onto the surface membranes, the number of proteins being synthesized per second and how many ribosomes are needed to do so. Also, estimate the number of carbon atoms it takes to make a bacterium and use that estimate to make a lower bound estimate on the rate of sugar uptake by a growing bacterium.

(b) In this case, think about the motility of the bacterium *Listeria monocytogenes* and a typical eukaryotic cell. In the case of *Listeria*, the motion of the bacterium is mediated by the formation of actin comet tails which depend in turn upon the linear polymerization of actin filaments. The formation of the actin comet results in a speed for the bacterium of something around 0.1 μm/sec. In the eukaryotic setting, the cell extends arms called filopodia which permit it to crawl, again by virtue of actin polymerization. For *Listeria*, use the measured rate of motion of the bacterium to *estimate* the rate of actin polymerization both in microns/sec and monomers/sec. Make sure you draw a picture of the process and explain your rationale. Now, take that estimate for the rate of actin polymerization and estimate the rate at which a filopodium extends on a eukaryotic cell. Anything you can do to compare these estimates with measurements would be useful - one excellent source is **Cell Movements** by Dennis Bray.

(c) Look at fig. 6-9 of *Essential Cell Biology* and assuming that this is a representative sample of the replication process, estimate the number of DNA polymerase molecules in a eukaryotic cell like this one from the fly. Note that the fly DNA is about 1.8×10^8 nucleotide pairs in size. Estimate the fraction of the total fly DNA shown in the micrograph. There are eight forks in the micrograph, numbered 1-8. Estimate the lengths of the DNA strands between replication forks 4 and 5 where we count the forks from left to right. If a replication fork moves at a speed of 100 nucleotides/s, how long will it take for forks 4 and 5 to collide. Also, given the mean spacing of the bubbles, estimate how long it will take to replicate the entire fly genome.